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Keywords:	Hypertension, Cardiovascular diseases, Aircraft noise, Cohort study

Is aircraft noise exposure associated with cardiovascular disease and hypertension? Results from a cohort study in Athens Greece

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Abstract

Background: We followed up, in 2013, the subjects who lived near the Athens International Airport and had participated in the cross-sectional multi-country HYENA study in 2004-06.

Objectives: The objective was to evaluate the association of exposure to aircraft and road traffic noise with the incidence of hypertension and other cardiovascular outcomes.

Methods: From the 780 individuals who participated in the cross-sectional study, 537 were still living in the same area and 420 accepted to participate in the follow-up. Aircraft and road traffic noise exposure was based on the estimations conducted in 2004-06, linking geo-coded residential addresses of the participants to noise levels. We applied multiple logistic regression and Cox proportional hazards models, adjusting for potential confounders.

Results: The incidence of hypertension was significantly associated with higher aircraft noise exposure during the night. Specifically, the OR for hypertension per 10 dB increase in Lnight aircraft noise exposure was 2.63 (95% C.I. 1.21-5.71). Doctor diagnosed cardiac arrhythmia was significantly associated with Lnight aircraft noise exposure, when prevalent and incident cases were considered with an OR of 2.09 (95% CI 1.07, 4.08). Stroke risk was also increased with increasing noise exposure but the association was not significant. Twenty four hour road traffic noise associations with the outcomes considered were weaker and less consistent.

Conclusions: In conclusion, our cohort study suggests that long-term exposure to aircraft noise, particularly during the night is associated with incident hypertension and possibly, also, cardiovascular effects.

Keywords: Hypertension, Cardiovascular diseases, Aircraft noise, Cohort study

What this paper adds
• Cardiovascular health impacts of transportation-related noise are a growing concern among general public, especially concerning the effects of road traffic noise.
• We report the results of a follow-up study in Greece, aiming to assess the incidence of hypertension and cardiovascular outcomes in relation to noise exposure.
• The findings of this study suggest that long-term exposure to aircraft noise, particularly during the night is associated with incident hypertension and possibly, also, cardiovascular effects.
• We anticipate that the research undertaken will be useful for improving the quality of public health in areas where exposure to transportation-related noise is prevalent.

Word count: 3,451

INTRODUCTION

There is ample evidence for auditory effects of exposure to occupational, social and road traffic noise. Exposure to noise has also been associated with annoyance/sleep disturbance [1]. Evidence is accumulating concerning effects related to increased prevalence or incidence of cardiovascular disease and hypertension and effects on cognitive performance in children[2-4]. Much of the evidence relies on cross-sectional studies, but some longitudinal epidemiological studies have been implemented especially concerning the effects of road traffic noise[5, 6]. Regarding noise from aircrafts, which affects populations residing near large airports, a smaller number of studies have reported results. The cross-sectional HYENA study, which included inhabitants near six large European airports, was the first European multi-city reporting effects of night time aircraft noise on the prevalence of hypertension[7] which was independent of the annoyance levels[8]. Some studies also reported acute effects of noise exposure on elevated BP measurements[9]; an increase in morning salivary cortisol in women exposed to aircraft noise[10] and a suggestive association of aircraft noise with the use of antihypertensive medication[11]. Other ecological studies have found evidence of associations with cardiovascular disease endpoints[12-15]. Short term experimental studies reported evidence for effects of night-time aircraft noise on next day blood pressure and arterial stiffness[16, 17].

The inhabitants around the Athens International Airport "Eleftherios Venizelos" (AIA) formed one of the six groups studied within the context of the HYENA study. The representative population sample included 780 individuals and the fieldwork took place in 2004-6. In this paper we report the results of a follow-up study, in 2013, in the same individuals, aiming to assess the incidence of hypertension and cardiovascular outcomes in relation to noise exposure.

SUBJECTS AND METHODS

Study population and health outcomes

AIA is located west of the Municipality of Artemida about 20 km to the east of central Athens. The airport can handle 600 take-offs and landings per day. From the planning stage of the AIA (which started its operation in 2001), it was acknowledged that noise would affect the population of Artemida, thus, the HYENA study subjects were sampled from this population (a total of 21,488 inhabitants; Hellenic Statistical

Authority Census 2011). In order to sample subjects for the HYENA study ensuring noise exposure contrasts, predicted noise curves were obtained from the Airport. The modeling used for aircraft noise is based on Integrated Noise Model (INM) [18]. Based on these predictions, noise contours were drawn over the map of the study area and the area which was subsequently divided in three zones according to noise levels: <50dB, 50-60dB and >60dB. Fifteen percent, 50% and 35% of subjects were sampled from each category respectively.

Between January and September 2013, two qualified and trained interviewers visited the households of all 780 individuals who participated in the 2004-6 HYENA study. Seventy eight individuals had died (information was obtained from members of their household or from neighbours), 76 had moved (information from the neighbours) and 89 could not be found. Thus 537 individuals were identified alive and living in the same area, and among them 420 (78%) accepted to participate in the follow-up study. There was slightly better participation (82%) in highest vs. lowest noise exposure categories (72% - see also Supplemental material: Table S1). Differences in demographic characteristics, life style, occupational status and household characteristics between individuals that agreed to participate in the follow-up study and non-participating residents at baseline (2004 - 2006) are shown in Table S2. Figure 1 presents the residential locations of the 420 participants. Those who agreed to participate were visited at home and a questionnaire with information on health events during the follow-up study (January to September 2013) (including incidence of hypertension, CVD, diabetes, lifestyle, occupation and annoyance following the original HYENA questionnaire) and household characteristics (including changes to protect from noise exposure) was completed by interview. Blood pressure was measured according to the initial HYENA protocol[7, 19] by specially trained staff who assessed BP at home visits. The study definition of hypertension[7] included individuals who had either BP levels above the WHO cutoff points (systolic BP ≥140 mmHg or diastolic BP≥90 mmHg), [20] and/or a diagnosis of hypertension (by a physician) and were using antihypertensive medication, as reported in the interview questionnaire.

Noise exposure assessment

Exposure to aircraft and road traffic noise for each individual, based on the location of their residence, was used as estimated at the baseline [7, 19]. For the assessment of

aircraft noise, the SONDEO existing noise model engine was used[18]. The noise and performance databases are those provided by the INM, Version 6.1). The INM [18] was used in the study area to assess personal aircraft noise exposure. Modeled noise exposure levels were linked to each participant's home address using geographic information systems[21].

To assess the effect of noise exposure on cardiovascular disease endpoints and hypertension, we used the A-weighted equivalent continuous noise level over T hours (LAeq,T) as the exposure indicator recommended by WHO [22] For aircraft noise, the indicators LAeq,16hr (day defined as the hours between 0700 and 2300) and Lnight (night defined as the hours between 2300 and 0700) were used to differentiate the effects of daytime and night-time exposure.

Annoyance and other possible effect modifiers

Noise annoyance (separately for the time of the day: during daytime and night-time; and also separately by source: from aircrafts and road traffic) was assessed, following the HYENA questionnaire, through personal interviews using the 11-point 'ICBEN scale' ranging from 0 to 10 [23]. The association of annoyance and hypertension was evaluated, as well as the role of annoyance as mediator and potential effect modifier (categorized into 2 levels (0–7 vs 8–10) of the noise exposure-hypertension association. We evaluated possible effect modification patterns for the annoyance-hypertension association by window opening habits (always closed vs sometimes open), time spent in the living room on workdays (dichotomized by the median: ≥ 9vs < 9 hours), time spent in the bedroom on workdays (dichotomized by the median: ≥ 8 vs < 8 hours), noise reducing remedies (yes vs no) and building modifications to reduce the noise (yes vs no).

Statistical analysis

We applied multiple logistic regression models to investigate the risk of hypertension and cardiovascular (CVD) outcomes, including cardiac arrhythmia, myocardial infarction, stroke and diabetes following long-term noise exposure. We also analysed self-reported hearing problems and doctor diagnosed hearing impairment as outcome variables. Two multiple logistic regression models were applied for each health outcome: a) including all subjects regardless of whether they were prevalent cases at

baseline and b) excluding the prevalent cases at baseline. We also applied a Cox proportional hazards model to take into account the time of diagnosis for hypertension, the most frequent outcome. Person years were assumed from baseline until the year of the diagnosis for the specific outcome.

In all the models, we adjusted for gender (males vs females), age (years), smoking habits (yes vs no), body mass index (BMI; kg/m^2), educational level (quartiles of years in education), physical activity (duration and intensity: less than once a week, 1-3 times a week and > 3 times a week), alcohol intake per week (number of units, where 1 unit = 10 mL pure ethanol) and salt intake (always adding salt to food at the table vs sometimes, seldom or never) at baseline. We evaluated the sensitivity of our findings for hypertension by including noise exposure at work (defined as "having to raise voice in order to communicate") in all models.

As the noise exposure variables, LAeq,16hr and Lnight , were highly correlated in our study area (r=0.70), they were included alternatively in the models. LAeq,24hr was used as the exposure variable for road traffic noise. The correlation between LAeq,24hr road traffic noise and Lnight, LAeq,16hr was 0.08 and 0.44 respectively. Aircraft and road traffic noise exposure indicators were not simultaneously introduced in the models.

To assess effect modification, an interaction term of each potential effect modifier with the relevant noise exposure indicator was included in the model.

We conducted mediation analysis[24] to identify whether annoyance was a mediator in the noise-hypertension association (i.e. if it is a step in the causal chain- entirely or partly responsible for the effect) and to quantify the extent to which the effect of exposure to aircraft noise levels on hypertension was mediated through annoyance. There are 3 steps in conducting mediation analysis: 1) by applying a multiple logistic regression model with hypertension as the outcome variable Y, Lnight aircraft noise as the causal variable X and adjusting for the potential confounders mentioned above; 2) by applying a multiple linear regression model in which the potential mediator variable M (annoyance from aircraft noise) is treated as the dependent variable, the causal variable (Lnight) as an independent variable and controlling for the same confounders;

and 3) by regressing Y on X and M and adjusting for the same confounders. For this purpose we used the "medeff" command in STATA version 13. The quasi-Bayesian Monte Carlo algorithm[25] was applied to test the indirect effect, to determine the significance of mediation effects and compute the proportion of the total variance mediated. We report the proportion of total effects mediated, the average mediation effect and the corresponding 95% CIs.

RESULTS

Table 1 shows personal and household characteristics of the 420 participants. Smoking and alcohol drinking have decreased over the follow-up period. More participants, in total 57.6% reached retirement age at follow up. Noise reducing remedies and building modifications to reduce noise also decreased over the follow-up period. Moreover, 99.8% of the participants were white and 72 (17.1%) were employed at the airport at baseline.

Table 1. Personal and household characteristics of 420 participants in the baseline (2004-2006) and the follow-up study (2013).

Personal & Household characteristics	At baseline	At follow-up
Age (mean, SD; years)	58 (9.1)	67 (9.1)
Gender (n,%; male)	186 (44.3)	186 (44.3)
Years of education (mean, SD)	10 (4.2)	10 (4.2)
Current smokers (n,%)	155 (63.6)	108 (41.2)
Number of alcoholic drinks/week (mean, SD)	6 (10.4)	3.5 (6.3)
Adding salt to food at the table: Always/sometimes (n,%)	125 (29.8)	120 (28.6)
Seldom/never (n,%)	293 (69.8)	298 (71.4)
Moderate exercise: Never (n;%)	45 (10.7)	73 (17.4)
Not regularly (n,%)	66 (15.7)	72 (17.1)
1-3 times/month (n,%)	11 (2.6)	27 (6.4)
1-3 times/week (n,%)	62 (14.8)	83 (19.8)
4-6 times/week (n,%)	40 (9.5)	69 (16.4)
Every day (n,%)	187 (44.5)	92 (21.9)
Occupational status: working (n,%)	134 (31.9)	58 (13.8)
unemployed (n,%)	4 (1.0)	17 (4.0)
home duties/carer (n,%)	121 (28.8)	100 (23.8)
retired (n,%)	161 (38.3)	242 (57.6)
Exposed to noise at work** (n,%)	21 (5.0)	8 (1.9)
Time living in the present home (years; mean, SD)	11 (7.8)	19 (7.8)
Bedroom windows open vs always closed (n,%)	371 (88.3)	412 (98.1)
Living room windows open vs always closed (n, %)	344 (81.9)	349 (83.1)
Time spent in the bedroom on workdays	264 (62.9)	272 (64.8)

≥8h vs <8h (n,%)		
Time spent in the living room on workdays ≥9h vs <9h (n, %)	81 (19.3)	214 (51.0)
Noise reducing remedies* during the night (n,%)	252 (60.0)	158 (37.6)
Noise reducing remedies* during the day (n,%)	263 (62.6)	139 (33.1)
Building modifications to reduce the noise (n,%)	92 (21.9)	51 (12.1)

*Ear plugs, closing windows, closing window shutters, other or any yes/no
** Having to raise voice in order to communicate

Table 2 presents the distribution of participants in the noise exposure categories at baseline. Most residents (68.4%) are exposed to a level of 50 to 60 dB regarding LAeq16, hr aircraft noise, 45.7% are exposed to Lnight aircraft noise between 40 and 45 dB, while 49.3% of the participants are exposed to road traffic noise less than 40 dB. Table S3 presents the distribution of annoyance. Annoyance levels from aircraft noise decreased during the follow-up period. None reported annoyance from road traffic, trains, construction, industry, neighbours, commercial activity, indoor installations or any other noise source.

Table 2. Distribution of the 420 participants in the exposure categories according to the noise exposure indicators (per 5dB) at baseline.

Exposure categories per 5dB	**LAeq,16hr aircraft (dB)**	**Lnight aircraft (dB)**	**LAeq,24hr road traffic (dB)**
< 30	0 (0)	0 (0)	118 (28.1)
30 - 35	0 (0)	45 (10.7)	40 (9.5)
35 - 40	48 (11.4)	69 (16.4)	49 (11.7)
40 - 45	27 (6.4)	192 (45.7)	71 (16.9)
45 - 50	13 (3.1)	112 (26.7)	59 (14.0)
50 - 55	144 (34.3)	2 (0.5)	37 (8.8)
55 - 60	143 (34.1)	0 (0)	26 (6.2)
≥ 60	45 (10.7)	0 (0)	20 (4.8)
mean (SD)	*52.9 (6.97)*	*42.0 (4.38)*	*38.7 (12.56)*

Lnight aircraft: A-weighted equivalent continuous aircraft noise level over the night (night defined as the hours between 2300 and 0700)
LAeq,16hr aircraft: A-weighted equivalent continuous aircraft noise level over the day (day defined as the hours between 0700 and 2300)
LAeq,24hr road traffic: A-weighted equivalent continuous road traffic noise level over 24 hours

Table 3 shows the number of prevalent and incident cases for the health outcomes studied. During the follow-up study there were over 40 newly diagnosed cases of

hypertension, doctor diagnosed cardiac arrhythmia, self reported hearing problems and doctor diagnosed hearing impairment.

Table 3. Prevalent (at baseline) and incident cases for the health outcomes studied in 420 study participants.

	Prevalent cases at baseline n (%)	**Incident cases during follow-up n (%)**
Hypertension*	194 (46.2)	71 (16.9)
Doctor diagnosed cardiac arrhythmia	24 (5.7)	44 (10.5)
Doctor diagnosed myocardial infarction	16 (3.8)	18 (4.3)
Doctor diagnosed stroke	7 (1.7)	5 (1.2)
Doctor diagnosed diabetes	41 (9.8)	30 (7.1)
Self reported hearing problems	63 (15.0)	81 (19.3)
Doctor diagnosed hearing impairment	31 (7.4)	43 (10.2)

*as defined by doctor diagnosis and medication use and/or high blood pressure measurements during the interview

Table 4 presents the effect estimates for noise levels and health outcomes. Exposure to aircraft noise, especially night-time, was associated to total and incident hypertension. Specifically, the odds ratio (OR) for hypertension per 10dB Lnight aircraft noise exposure increase when all hypertension cases were included was 1.69 (95% C.I.: 1.01-2.82); the OR for incident hypertension associated with the same exposure was 2.63 (95% C.I.: 1.21-5.71). Doctor diagnosed cardiac arrhythmia was also associated with Lnight, but not with LAeq,16h, but the association reached statistical significance only when all cases were considered (i.e. prevalent at baseline and incident) with an OR of 2.09 (95% CI: 1.07-4.08). Stroke risk was also increased with increasing noise exposure at night but the association was not significant, maybe due to the very small number of cases. The OR for the incidence of self reported and doctor diagnosed hearing impairment per 10dB Lnight aircraft noise exposure was 1.97 (95% C.I.: 1.05-3.71) and 3.51 (95% C.I.: 1.46-8.44) respectively. The estimated hazard ratio (HR) for hypertension, when Cox regression was applied (Table S4), associated with a 10 dB increase in Lnight and LAeq,16hr was 3.39 (95% C.I.: 0.87-13.3) and 1.34 (95% C.I.: 0.57-3.16) respectively. Twenty four hour road traffic noise effect estimates were

weaker and less consistent. Our estimates were robust to adjustment of noise exposure at work.

Table 4. Odds ratios (OR) & 95% confidence intervals (C.I.) for hypertension and cvd outcomes associated with a 10dB increase in noise exposure at the subjects' residence.

Outcome	Noise exposure (per 10dB)	Model 1** OR 95%C.I.	Model 2** OR 95%C.I.
Hypertension*	Lnight aircraft	**1.69 (1.01,2.82)**	**2.63 (1.21,5.71)**
	LAeq,16hr aircraft	**1.45 (1.05,1.99)**	1.46 (0.89,2.39)
	LAeq,24hr road traffic	1.07 (0.90,1.27)	1.18 (0.92,1.52)
Doctor diagnosed cardiac arrhythmia	Lnight aircraft	**2.09 (1.07,4.08)**	1.88 (0.85,4.19)
	LAeq,16hr aircraft	1.28 (0.85,1.94)	1.33 (0.80,2.21)
	LAeq,24hr road traffic	1.01 (0.81,1.26)	0.96 (0.74,1.26)
Doctor diagnosed myocardial infarction	Lnight aircraft	0.83 (0.31,2.20)	0.37 (0.10,1.42)
	LAeq,16hr aircraft	1.03 (0.55,1.92)	0.69 (0.29,1.63)
	LAeq,24hr road traffic	0.89 (0.64,1.24)	0.96 (0.60,1.53)
Doctor diagnosed stroke	Lnight aircraft	1.30 (0.32,5.31)	1.99 (0.23,17.2)
	LAeq,16hr aircraft	0.84 (0.36,1.95)	1.02 (0.30,3.54)
	LAeq,24hr road traffic	0.93 (0.56,1.54)	1.33 (0.59,3.03)
Doctor diagnosed diabetes	Lnight aircraft	1.09 (0.58,2.07)	0.92 (0.35,2.44)
	LAeq,16hr aircraft	0.95 (0.64,1.41)	0.87 (0.48,1.58)
	LAeq,24hr road traffic	1.00 (0.80,1.24)	1.18 (0.85,1.65)
Self reported hearing problems	Lnight aircraft	1.47 (0.88,2.47)	**1.97 (1.05,3.71)**
	LAeq,16hr aircraft	1.23 (0.89,1.70)	1.39 (0.93,2.07)
	LAeq,24hr road traffic	1.13 (0.95,1.34)	1.05 (0.86,1.29)
Doctor diagnosed hearing impairment	Lnight aircraft	**2.04 (1.06,3.91)**	**3.51 (1.46,8.44)**
	LAeq,16hr aircraft	**1.75 (1.13,2.70)**	**2.33 (1.26,4.30)**
	LAeq,24hr road traffic	0.98 (0.80,1.21)	1.01 (0.78,1.32)

*as defined by doctor diagnosis and medication use and/or high blood pressure measurements during the interview

** Model 1:Logistic regression including prevalent and incident cases of hypertension; Model 2:Logistic regression including only incident cases (both after adjusting for age, sex, BMI, alcohol intake, education, exercise, smoking habits and salt intake at baseline)

Lnight aircraft: A-weighted equivalent continuous aircraft noise level over the night (night defined as the hours between 2300 and 0700)

LAeq,16hr aircraft: A-weighted equivalent continuous aircraft noise level over the day (day defined as the hours between 0700 and 2300)

LAeq,24hr road traffic: A-weighted equivalent continuous road traffic noise level over 24 hours

Annoyance from aircraft and road traffic noise was moderately correlated with actual noise levels (Spearman r's 0.20-0.45; P <0.001). Table 5 shows the estimates of the effects of noise exposure and annoyance on hypertension, entered individually in the models and mutually adjusted. Higher annoyance scores were associated with slightly increased risk of hypertension but only the association between annoyance (not "high

annoyance") during the day reached statistical significance. When adjusted mutually, the effect estimates for noise exposure, especially during the night, more robust compared to those of annoyance, as the OR for incident hypertension was 2.61 (95% C.I.: 1.19-5.70) per 10dB increase in Lnight. Annoyance was not significantly associated with hypertension.

Table 5. Odds ratio (OR) & 95% confidence intervals (C.I.) of hypertension* associated with a 10 dB increase in aircraft noise level, one unit increase in the 11-point scale aircraft noise annoyance scale and aircraft noise high annoyance (dichotomous variable: highly annoyed defined from categories 8,9,10 on the 11 point scale vs all other). Model 1: Logistic regression including prevalent and incident cases of hypertension; Model 2: Logistic regression including only incident cases.

Variables in the model	**Model 1** OR 95% C.I.**	**Model 2** OR 95% C.I.**
Included alternatively		
Lnight from aircraft (10 dB)	**1.69 (1.01, 2.82)**	**2.63 (1.21, 5.71)**
LAeq,16hr from aircraft (10 dB)	**1.45 (1.05, 1.99)**	1.46 (0.89, 2.39)
Annoyance from aircraft noise during the night (11-point scale)	1.04 (0.98, 1.11)	1.03 (0.95, 1.12)
Annoyance from aircraft noise during the day (11-point scale)	**1.07 (1.00, 1.14)**	1.10 (0.99, 1.22)
Highly annoyed** from aircraft noise during the night (yes vs no)	1.04 (0.66, 1.62)	1.17 (0.63, 2.19)
Highly annoyed** from aircraft noise during the day (yes vs no)	1.33 (0.86, 2.06)	1.38 (0.74, 2.58)
Mutually adjusted		
Lnight from aircraft (10 dB) Annoyance from aircraft noise during the night (11-point scale)	1.58 (0.93, 2.69) 1.03 (0.97, 1.09)	**2.58 (1.17, 5.70)** 1.01 (0.93, 1.10)
LAeq,16hr from aircraft (10 dB) Annoyance from aircraft noise during the day (11-point scale)	1.33 (0.92, 1.92) 1.04 (0.96, 1.12)	1.24 (0.70, 2.17) 1.08 (0.96, 1.21)
Lnight aircraft (10 dB) and Highly annoyed*** from aircraft noise during the night (yes vs no)	**1.70 (1.01, 2.85)** 0.97 (0.62, 1.53)	**2.61 (1.19, 5.70)** 1.06 (0.56, 2.01)
LAeq,16hr aircraft (10 dB) and Highly annoyed*** from aircraft noise during the day (yes vs no)	**1.40 (1.00, 1.97)** 1.13 (0.70, 1.80)	1.39 (0.83, 2.35) 1.20 (0.62, 2.32)

*as defined by doctor diagnosis and medication use and/or high blood pressure measurements during the interview

**adjusting for age, sex, BMI, alcohol intake, education, exercise, smoking habits and salt intake at baseline

***categories 8,9,10 versus all others on the 11 point scale (range: 0 to 10)

Lnight aircraft: A-weighted equivalent continuous aircraft noise level over the night (night defined as the hours between 2300 and 0700)

LAeq,16hr aircraft: A-weighted equivalent continuous aircraft noise level over the day (day defined as the hours between 0700 and 2300)

Using mediation analysis (Table S5), the effect estimate of aircraft noise exposure on hypertension (all cases and incident only) was not mediated by annoyance to aircraft noise. The indirect effect represented the 14.2% and 1.6% of the total effect during the night time, for all cases and incident only, respectively. The percent of the total effect mediated by annoyance during the day was higher; 24.1% (all cases) and 8.2% (incident cases). No statistically significant effect modification of the noise exposure-hypertension association by annoyance was observed (p-value>0.05).

DISCUSSION

In this prospective cohort study we observed elevated risks for hypertension, arrhythmia and stroke associated to aircraft noise exposure, especially during the night. No association was observed between noise exposure and the risk of MI or diabetes. Using mediation analysis, annoyance to noise did not explain the noise effect on hypertension.

We used hypertension as the primary health outcome and also investigated the association with other cardiovascular outcomes including time of diagnosis. The cross-sectional HYENA study[7] reported an OR of 1.14 per 10dB increase in Lnight, lower than that observed here in this follow-up of a subset of the cohort. The reason for this discrepancy may lie in the study design (the older cross-sectional design was more prone to biases) and also in the fact that the population of our cohort is now older and subjects have lived for much longer in the vicinity of the airport. There is evidence that length of stay is associated with the occurrence of hypertension and heart disease[26, 27], a fact that may reflect either the lag needed or the necessary cumulative exposure to influence the outcome[28].

The majority of studies on the health effects of noise exposure concern hypertension with few studies on aircraft noise. However, most studies find results broadly consistent to ours. De Souza et al[29], in an occupational noise exposure study at higher noise exposure levels (>75dB) and including younger subjects compared to the present study,

found an OR for hypertension of 1.56 (95% C.I.: 1.13-2.17). A recent meta-analysis of 5 studies on the effect of noise on the prevalence/incidence of hypertension[6], which did not include the HYENA study, found an OR of 1.63 for exposure to aircraft noise vs non-exposure, a finding consistent with ours (although it should be noted that the definition of "exposure" was differently defined between studies). The meta-analysis by Van Kempen & Babisch[5], which included cross-sectional studies, found an OR between road traffic noise and hypertension equal to 1.034 (95% C.I.: 1.011-1.056) per 5dB increase of the LAeq16hr. Meline et al[30], in a cross sectional study, investigated the associations of outdoor road, rail and air traffic noise, estimated at the place of residence and workplace with BP measurements and the assessment of hypertension. However, only noise estimated at the workplace was associated with elevated BP.

There are a few studies in the literature which have examined the association between long-term aircraft noise exposure and mortality or hospitalizations for cardiovascular diseases providing some evidence for adverse effects of noise exposure. In the original HYENA study[27] an association was found between Lnight aircraft noise and combined heart disease and stroke for participants who had lived in the same place for ≥ 20 years (OR=1.25 with 95% C.I.: 1.03-1.51) per 10dB. In the Heathrow study[12], hospital admissions showed linear trends of increasing risk with higher levels of day and night aircraft noise. Huss et al[26] reported a 30% increase mortality by from MIs in individuals exposed to >60dB compared to those exposed to <45dB aircraft noise in Switzerland and found the length of stay to be an important determinant of risk. Evrard et al[14], in an ecological study in 161 French communes near three major airports, found increased mortality by 18% from CVD, 24% from CHD, 28% for MI and 8% for stroke per 10dB increase in Lden aircraft noise.

Vienneau et al[31], in a meta-analysis of 10 studies, examined the association of the combined exposure to road and aircraft noise on the incidence of ischemic heart disease and found an increased risk by 6% per 10dB increase in noise exposure starting at a level of 50dB. Halonen et al[32] found an 5% and 9% increased risk for hospital admissions in adults and elderly individuals living in areas with >60dB daytime road traffic noise exposure versus areas with <55dB. Kälsch et al[33] evaluated the effect of road traffic noise exposure on the thoracic aortic calcification and found a 3.9% increase per 5dB in Lnight, showing possible early effects of noise exposure on atherosclerosis.

Schmidt et al[16] in an experimental study were able to identify small changes in pathophysiological mechanisms in 75 healthy volunteers with small cardiovascular risk. Also, in another experimental study[17] they found that nighttime aircraft noise markedly impaired the endothelial function in 60 patients with or at risk for cardiovascular disease.

Our study was able to analyze the association of long-term exposure to noise from aircrafts with the prevalence and incidence of self reported doctor diagnosed cardiac arrhythmia, MI, stroke and diabetes and we found an increased risk for arrhythmia and stroke but no association with MI and diabetes. We are not aware of other studies that have assessed arrhythmia. Our results for stroke are broadly consistent with the few other reported results but for MI they are not consistent with previously reported findings[31]. Reasons for this discrepancy might be the small number of cases in our study and the different exposure levels and sources of noise.

Following the HYENA study, we assessed noise annoyance in our follow up study. Annoyance to noise has been identified as an independent predictor of hypertension in a few studies[34, 35]. However the evidence from the cross-sectional HYENA study showed that noise exposure is a more important risk factor for hypertension compared to annoyance[8]. Investigation of the role of annoyance as an effect modifier of the noise exposure-hypertension association gave inconsistent results[36-38]. In our analysis of incident cases of hypertension we found consistent results with the previous HYENA cross-sectional analysis, i.e. we found noise exposure to be a more important predictor of the risk for incident hypertension compared to annoyance and we found no significant effect modification. In the mediation analysis applied, our finding suggests that there was a noise-hypertension effect independent of annoyance, and the estimated indirect effect was not statistically significant.

In the present study we also found an effect of long-term exposure to aircraft noise and hearing problems. However, according to the literature these noise levels are relatively low and likely not associated with such effects[22]. One possible explanation may be that persons with hearing problems are less annoyed and have a smaller probability of moving away from a noisy area.

Among the advantages of our study is the longitudinal study design. Few studies assessing noise exposure effects from aircraft have been cohort studies to date. Another advantage is the high response rate (78%). The response rate was dependent on the noise exposure (72% in the low exposed subjects compared with 82% in the highly exposed subjects). However, the high response rate in subjects of both exposure categories, means that this difference likely did not affect the estimates. Additionally, an advantage is that we were able to study effects from aircraft noise exposure in an area with very low road traffic noise. Also, we were able to look at potential effect modification resulting from noise annoyance.

An important limitation was our inability to study cause-specific mortality in relation to noise exposure. Although 78 subjects died during the follow up, we were not able to examine death certificates as we had no consent for that. A further disadvantage of our study was the relatively small number of subjects which reduced the statistical power. The high prevalence of hypertension (63%) ensures enough power to detect an effect, however, other CVD health outcomes had a much smaller prevalence (16%, 8%, 3%, 17% for arrhythmia, myocardial infarction, stroke and diabetes respectively). In our study we did not adjust for air pollution levels as the area has no monitors allowing the assessment of geographical variations. However, there is evidence that adjusting for air pollutants does not attenuate the noise effects[14, 31]. We relied on ambient noise models, and there may be differential attenuation of noise penetrating indoors due to building characteristics and window-opening.

In conclusion our cohort study suggests that long-term exposure to aircraft noise, particularly night-time, is associated with incident hypertension and possibly CVD effects.

Contributorship:

Konstantina Dimakopoulou made substantial contributions to conception and study design and analysis and interpretation of data, drafted the article and revised it critically for important intellectual content and approved the final version to be published.

Konstantinos Koutentakis made substantial contributions to acquisition of the data, critically revised the article for important intellectual content and approved the final version to be published.

Ifigeneia Papageorgiou made substantial contributions to acquisition of the data, critically revised the article for important intellectual content and approved the final version to be published.

Maria-Iosifina Kasdagli made substantial contributions to analysis and interpretation of data, critically revised the article for important intellectual content and approved the final version to be published.

Alexandros S Haralabidis made substantial contributions to conception and study design and revised it critically for important intellectual content and approved the final version to be published.

Panayota Sourtzi made substantial contributions to conception and study design and revised it critically for important intellectual content and approved the final version to be published.

Evangelia Samoli made substantial contributions to conception and study design and revised it critically for important intellectual content and approved the final version to be published.

Danny Houthuijs made substantial contributions to conception and study design and revised it critically for important intellectual content and approved the final version to be published.

Wim Swart made substantial contributions to conception and study design and revised it critically for important intellectual content and approved of the final version to be published.

Anna L Hansell made substantial contributions to conception and study design, drafted the article and revised it critically for important intellectual content and approved the final version to be published.

Klea Katsouyanni made substantial contributions to conception and study design, drafted the article and revised it critically for important intellectual content and approved the final version to be published.

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Figure Legend

Figure 1. Residential locations of the 420 individuals who participated in the 2013 follow-up study, by estimated aircraft noise exposure levels at baseline. AIA: Athens International Airport. The runway is colored in yellow.

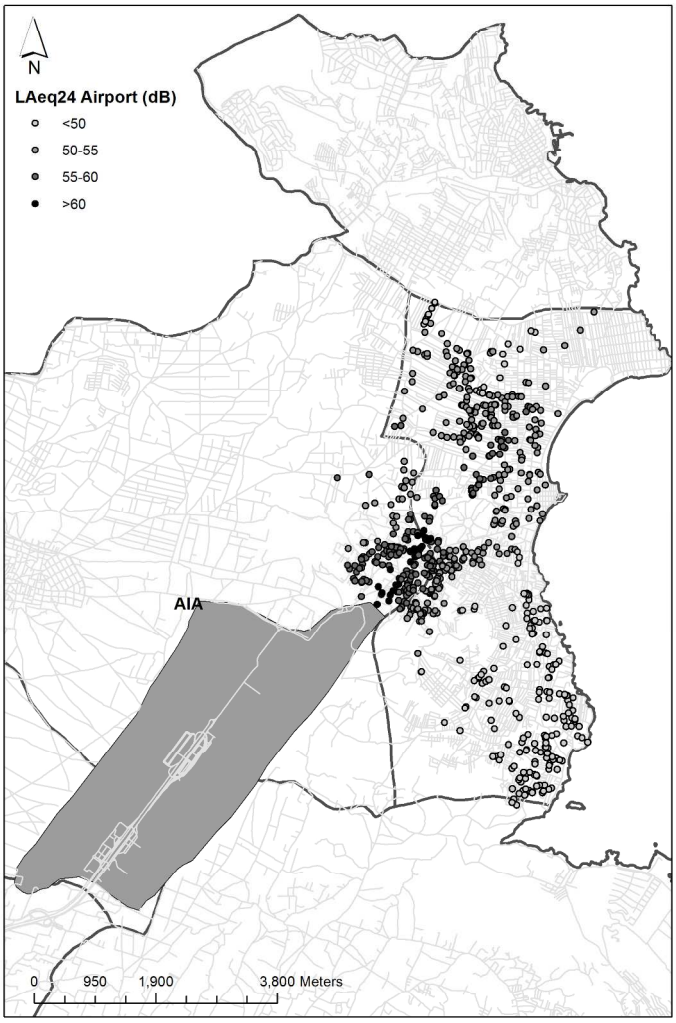

Figure 1

210x296mm (300 x 300 DPI)

Is aircraft noise exposure associated with cardiovascular disease and hypertension? Results from a cohort study in Athens Greece

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Supplementary material

Table S1. Response rate in the 2013 follow-up study according to noise exposure category.

Aircraft noise exposure (db)	Total number of individuals from the 2004-6 sample which were identified	Accepted to participate in the 2013 follow-up	Percent acceptance
<50	99	71	72
50-60	267	209	78
>60	171	140	82
All	537	420	78

Table S2. Personal and household characteristics of 420 individuals that agreed to participate in the follow-up study and 360 non-participating residents at baseline (2004-2006).

Personal & Household characteristics		Participants in follow-up study	Non-Participants
Age (mean, SD; years)		58 (9.1)	61 (9.6)
Gender (n,%; male)		186 (44.3)	183 (50.8)
Years of education (mean, SD)		10 (4.2)	10 (4.7)
Current smokers (n,%)		155 (63.6)	230 (64.4)
Number of alcoholic drinks/week (mean, SD)		6 (10.4)	5 (8.3)
Adding salt to food at the table:	Always/sometimes (n,%)	125 (29.8)	42 (11.8)
	Seldom/never (n,%)	293 (69.8)	315 (88.2)
Moderate exercise:	Never (n;%)	45 (10.7)	45 (12.5)
	Not regularly (n,%)	66 (15.7)	73 (20.3)
	1-3 times/month (n,%)	11 (2.6)	6 (1.7)
	1-3 times/week (n,%)	62 (14.8)	63 (17.5)
	4-6 times/week (n,%)	40 (9.5)	22 (6.1)
	Every day (n,%)	187 (44.5)	143 (39.7)
Occupational status:	working (n,%)	134 (31.9)	103 (28.6)
	unemployed (n,%)	4 (1.0)	7 (1.9)
	home duties/carer (n,%)	121 (28.8)	82 (22.8)
	retired (n,%)	161 (38.3)	164 (45.6)
Exposed to noise at work** (n,%)		21 (5.0)	21 (5.8)
Time living in the present home (years; mean, SD)		11 (7.8)	12 (9.6)
Bedroom windows open vs always closed (n,%)		371 (88.3)	317 (88.1)
Living room windows open vs always closed (n, %)		344 (81.9)	313 (86.9)
Time spent in the bedroom on workdays ≥8h vs <8h (n,%)		264 (62.9)	265 (73.6)
Time spent in the living room on workdays ≥9h vs <9h (n, %)		81 (19.3)	198 (55.0)
Noise reducing remedies* during the night (n,%)		252 (60.0)	118 (32.8)
Noise reducing remedies* during the day (n,%)		263 (62.6)	112 (31.1)
Building modifications to reduce the noise (n,%)		92 (21.9)	61 (16.9)

Noise exposure assessment

Noise levels for separate periods of the day were modeled for the subjects' residential addresses for the year 2002. For road traffic noise exposure, the Standaard Reken- en Meetvoorschrift (SRM) (RMW 2002) was used. In our study area road traffic is limited to three main roads and road traffic data were not available. Therefore vehicle counts were measured during different times of the day and different seasons of the year by vehicle type under the responsibility of the HYENA researchers and this information was used as input for the model.

Table S3. Distribution of annoyance scores of 420 participants at baseline and in the follow-up study.

Annoyance scores	At baseline	At follow-up
Bothered/disturbed/ annoyed by aircraft noise at daytime (scale from 0: not at all to 10: extremely), median 25-75th percentile	8 (5-10)	6 (1-9)
Bothered/disturbed/ annoyed by aircraft noise at nighttime (scale from 0: not at all to 10: extremely), median 25-75th percentile	6 (2-9)	3 (0-8)
Bothered/disturbed/ annoyed by air pollution/ smell/ odour /dust (scale from 0: not at all to 10: extremely), median 25-75th percentile	5 (0-9)	4 (0-8)
Number of highly annoyed to aircraft noise at daytime (categories 8,9,10 on the 11 point scale), n (%)	226 (53.9)	161 (38.4)
Number of highly annoyed to aircraft noise at nighttime (categories 8,9,10 on the 11 point scale), n (%)	158 (37.9)	117 (28.1)

Table S4. Hazard ratios (HR) & 95% confidence intervals (C.I.) for hypertension and cvd outcomes associated with a 10 dB increase in noise exposure at the residence of 420 subjects living near the Athens airport. Results from Cox regression models taking into account year of diagnosis.

Outcome	Noise exposure	HR 95% C.I.
Hypertension*	Lnight aircraft (10 dB)	3.39 (0.87, 13.3)
	LAeq,16hr aircraft (10 dB)	1.34 (0.57, 3.16)
	LAeq,24hr road traffic (10 dB)	1.01 (0.69, 1.50)
Doctor diagnosed cardiac arrhythmia	Lnight aircraft (10 dB)	1.39 (0.52, 3.70)
	LAeq,16hr aircraft (10 dB)	1.00 (0.52, 1.94)
	LAeq,24hr road traffic (10 dB)	0.73 (0.49, 1.08)
Doctor diagnosed myocardial infarction	Lnight aircraft (10 dB)	0.16 (0.01, 2.46)
	LAeq,16hr aircraft (10 dB)	0.21 (0.00, 5.16)
	LAeq,24hr road traffic (10 dB)	1.20 (0.50, 2.88)
Doctor diagnosed stroke	Lnight aircraft (10 dB)	NA only 5 incident cases
	LAeq,16hr aircraft (10 dB)	
	LAeq,24hr road traffic (10 dB)	
Doctor diagnosed diabetes	Lnight aircraft (10 dB)	0.95 (0.34, 2.63)
	LAeq,16hr aircraft (10 dB)	0.95 (0.52, 1.73)
	LAeq,24hr road traffic (10 dB)	1.09 (0.79, 1.50)
Self reported hearing problems	Lnight aircraft (10 dB)	NA, year not available
	LAeq,16hr aircraft (10 dB)	
	LAeq,24hr road traffic (10 dB)	
Doctor diagnosed hearing impairment	Lnight aircraft (10 dB)	NA, year of diagnosis not available
	LAeq,16hr aircraft (10 dB)	
	LAeq,24hr road traffic (10 dB)	

*as defined by doctor diagnosis and medication use and/or high blood pressure measurements during the interview

**adjusting for age, sex, BMI, alcohol intake, education, exercise, smoking habits and salt intake at baseline

Lnight aircraft: A-weighted equivalent continuous aircraft noise level over the night (night defined as the hours between 2300 and 0700)

LAeq,16hr aircraft: A-weighted equivalent continuous aircraft noise level over the day (day defined as the hours between 0700 and 2300)

LAeq,24hr road traffic: A-weighted equivalent continuous road traffic noise level over 24 hours

Table S5. Results of mediation analysis identifying the extent to which the effect of exposure to aircraft noise levels (X: casual variable) on hypertension (all cases and incident only), was mediated through annoyance (M: potential mediating variable).

All cases	X= Lnight from aircraft (dB) M= Annoyance from aircraft noise during the night	X= LAeq, 16hr from aircraft (dB) M= Annoyance from aircraft noise during the day
Average mediation effect & 95% CI	0.001 (-0.001, 0.004)	0.001 (-0.002, 0.004)
% of total effect mediated	14.2	24.1
Incident cases		
Average mediation effect & 95% CI	0.000 (-0.000, 0.004)	0.001 (-0.000, 0.003)
% of total effect mediated	1.6	8.2

Lnight aircraft: A-weighted equivalent continuous aircraft noise level over the night (night defined as the hours between 2300 and 0700)
LAeq,16hr aircraft: A-weighted equivalent continuous aircraft noise level over the day (day defined as the hours between 0700 and 2300)
*as defined by doctor diagnosis and medication use and/or high blood pressure measurements during the interview